Intracranial chondrosarcoma: review of the literature and report of 15 cases

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Abstract

The available data in the literature (177 cases), two current clinical patients, and cases which occurred in The Netherlands (13) were reviewed concerning the clinical presentation, pathological features, radiological data, and treatment options of chondrosarcoma of the cranial base.

The mean age of patients was 37 years, the male/female ratio 1: 1.1. The most frequent complaints were diplopia with oculomotor disorders (51%), headache (31%), and decreased hearing, dizziness, and tinnitus with statoacusticus dysfunction (21%). The mean duration of symptoms before diagnosis was 27 months.

The chondrosarcomas were located in the petrosal bone in 37% (47 cases), in the occipital bone and clivus in 23% (30 cases), in the sphenoïd bone in 20% (25 cases) and to a lesser extent in frontal, ethmoïdal, and parietal bones (14%). In 6% (eight cases) the primary location was in dural tissue. Radiological examinations showed bone destruction and variable calcification (CT), involvement of neuronal and vascular structures (MRI), and mostly hypovascularity on angiography. On histological examination 51% of tumours were classified as grade I, 11% grade II, 30% mesenchymal, and 8% myxoïd. The mesenchymal type was the most malignant as illustrated by a strong tendency to intradural and cerebral growth and possibly occurrence in younger age groups. The treatment of choice until recently was surgery because of the critical location and local aggressive nature. Regrowth of tumour after surgery occurred in 53% of the patients (average after 32 months). Charged particle irradiation gave a five year survival of 83–94% and a local control rate of 78%-91%. Both in surgery and radiotherapy there is treatment related morbidity and mortality that should be considered when offering these therapies.

Recent promising results imply that charged particle radiotherapy, in combination with surgery, may be the therapeutical choice of the future.

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Tumours originating from bone at the base of skull are rare. One such tumour, the chondrosarcoma, the most malignant cartilage tumour, represents 0.15% of all cranial space occupying lesions and 6% of all skull base tumours.[1] It is assumed that chondrosarcomas originate from remnants of embryonal cartilage or from metaplasia of meningeal fibroblasts.[2 3]

To the best of our knowledge, the last detailed review of the literature disclosed only 50 cases until 1985.[4] This led us to review the available literature since 1985 in detail. This report also concerns two of our own clinical patients and 13 other patients treated in different hospitals throughout The Netherlands. The clinical history, pathological features, radiological findings, and treatment options are discussed. From these data we give an overview of the current diagnostic procedures and therapeutic options of intracranial chondrosarcoma.

Methods

In addition to the study by Hassounah *et al*[4], analysis of the literature from 1985 disclosed 127 cases.[4–37] Our own two clinical patients and 13 other cases retrieved from the files of the Dutch Committee on Bone Tumours, University Hospital Leiden, and the reported cases since 1985 along with the 50 cases from the review of Hassounahet al[4] were analysed. Table 1 shows summarised data of the 15 Dutch patients.

Patients with chondrosarcoma from the nasopharynx or the paranasal sinus and extending into the skull base and chondrosarcoma as part of the syndromal diseases Maffuci or Ollier were excluded. The 27 patients of the series of Castro *et al* were also excluded because of paucity of detailed information.[38]

Results

The sex ratio was 1:1.1. In 16 cases, the sex of the patient was not reported. The average age was 37 years (range 3 months-76 years). Age was not reported in 67 cases.

Signs and symptoms at initial presentation were described in 67 patients (table 2). The median time period between initial symptoms and moment of diagnosis was 15 months (ranging from 1 month to 144 months). This information was available in only 36 cases.

Over the years, different radiological evaluation methods have been used. Plain skull radiography, CT, MRI, and angiography were the most often used diagnostic tools. On T1 weighted MRI, chondrosarcomas had a low to intermediate signal intensity and were isointense or hypointense to grey matter. On proton density and T2 weighted images, they had high signal intensity and were hyperintense to grey matter.[39]

Table 1 Characteristics of 15 Dutch patients

No	*Age/sex*	*Location*	*Pathology*	*Size*	*Symtoms/signs*
1	31/M	PS; extension in pons and in Scav; destruction of Ssph	Grade I	2½×3 cm	Headache 2 y; 1 y diplopia; sensory disturbance OD. Ptosis / VI dysfunction OD; cornea reflex R<L; sensory disturbance V branch 1 and 2 R
2	26/F	FM; SS	Grade I		Pain face 1 y; paraesthesias. V dysfunction L; possibly VII dysfunction L
3	18/F	PS; extension in clivus and SCav; petroclival junction	Grade II	1×2 cm	Several months diplopia on looking L; headache. VI dysfunction L
4	15/F	PS; extension in SSph	Grade I	3×2×2 cm	1 y Diplopia; headache. Dysfunction III L
5	23/M	PS; Clivus; SCav	Grade II		1 y Intermittent frontoparietal headache; diplopia horizontally. VI dysfunction R
6	72/M		Grade II		
7	38/M	Pontomedullary angle	Grade I		Dysfunction VII - XII R
8	33/M	Os petrosum	Grade II	3×2×2 cm	12 y Strabism; later unsteady gait and decreased hearing AD. Sensory disturbance V branch 2 R; paresis m trapezius and sternocleïdom. R; tongue deviating to R; dysdiadochokinesis and ataxia R
9	47/F	Behind os petrosum; extension to PS	Grade I	4×4×4 cm	
10	64/F	Cranial clivus; SS up to Monro	Grade I	4×4×6 cm	Hemiparesis R; disorder of speech; memory disturbance
11	72/F	Clivus; PS; Sphenoïd and SCav	Grade I		3½ y Decreased visual acuity OD; 3 months amaurosis OD and decreased visual acuity OS. Quadrant-anopsia and L VI dysfunction
12	45/M	FM and FP			
13	60/M	Petroclival			
14	44/M	Foramen jugulare and in tympanic cavity; Clivus and SCav	Grade II		2 Months pain R neck/ear; dizziness; nausea; decreased hearing and tinnitus AD; diplopia. Sensory disturbance R mouth, VII dysfunction R and hearing AD<AS
15	16/M	FM; Petrosal bone	Grade II		2 y Diplopia when looking R; paraesthesias maxillar and mandibular R, diplopia. No cornea reflex R; hypaesthesia V branch 1-2-3 R

PS = parasellar; FM = fossa media; FP = fossa posterior; SS = suprasellar; SCav = sinus cavernosus; SSph = sinus sphenoïdalis.

Intracranial tumour growth can be present. The origin has been reported to be in different bone parts (table 2). In eight cases an origin in the dura was described.

A pathological diagnosis was reported in 106 cases (table 2). Four subtypes of skull base chondrosarcomas were described in the literature: grade I, II, mesenchymal, and myxoïd type. No further pathological grading was given for mesenchymal and myxoid subtypes. The figure lists the pathological subtypes and their age of occurrence.

The extension in dural tissue of the chondrosarcoma, confirmed through postmortem data (10 cases) or radiological imaging only, was explicitly mentioned in 30 cases. Of these, 10 were diagnosed as chondrosarcoma grade I, three were diagnosed as grade II, 16 were diagnosed as mesenchymal type, and one as myxoïd.

Table 2 Clinical presentation, tumour location, and pathological subtypes of chondrosarcoma of the cranial base

		Cases	*(%)*
Symptoms/signs	Dysfunction of eye movement	37	51
	Headache	22	31
	Hearing loss, dizziness, and tinnitus	15	21
	Sensory disturbances of the face	15	21
	Decreased visual acuity	10	14
	Dysfonia	9	13
	Ataxia	8	11
	(Hemi)paresis	7	10
	Dysarthria/dysphagia	6	8
	Tongue paresis	6	8
	Facial palsy	6	8
	Nasal obstruction	3	4
	Decreased memory	3	4
	Nausea/vomiting	2	3
	Palatal mass	2	3
Bone parts	Os frontale	2	
	Os ethmoïdale	3	
	Os sphenoïdale	25	
	Os petrosum	47	
	Os pariëtale	13	
	Os occipitale or clivus	30	
	Origin in dura	8	
Subtypes	Grade I	54	51
	Grade II	12	11
	Grade III	0	
	Mesenchymal	32	30
	Myxoïd	8	8

The usual methods of treatment were neurosurgery and conventional or proton radiotherapy.[38 40 41] Stereotactic radiosurgery has been reported in only two cases.[22] Adjuvant chemotherapy was scarcely mentioned.[42]

A local recurrence rate of 53% after neurosurgical treatment (34 out of 64 cases) has been reported with clinical and radiological signs of regrowth after a mean interval of 32 months. In 40 cases information on the extent of the operation was reported: in 80% (32 cases) resection was subtotal and in 20% (eight cases) total.[4–37]

Thirteen of the 15 Dutch patients were operated on. Two received proton radiotherapy and one conventional radiotherapy postoperatively. Recurrence occurred in 54% (seven cases). The mean time to recurrence was three years. Recurrence free survival rates at 2, 3, and 5 years were calculated at respectively 67%, 56%, and 43%.

Discussion

This review of the literature and of our own cases (in total 192) illustrates the very low frequency of occurrence of intracranial chondrosarcoma. The incompleteness of data in the case reports is of such an extent that the clinical picture had to be made using a substantially smaller part of the published cases.

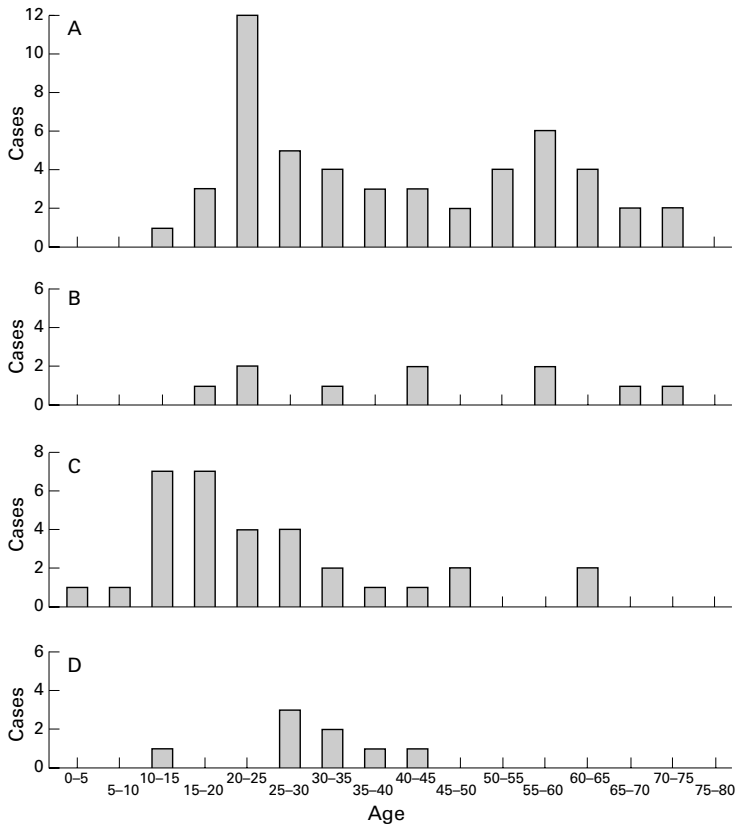
For patient characteristics, no sex dominance existed. The mean age was 37 years (our own series 43 years). Chondrosarcoma occurred in both very young and old age groups, from 3 months to 76 years of age. The mesenchymal subtype showed a tendency to occur at a younger age (figure).

The signs and symptoms at the first manifestation of the tumour were mainly caused by oculomotor dysfunction, related to

Table 1 continued

Invasion	*Postoperative course*
Dural and cerebral	Epilepsy and persisting VI dysfunction R; no recurrence after 10 y
	Pain maxillar and mandibular L, decreased hearing AS; recurrence after 2 y (operated)
	Mild III/VI dysfunction; twice reoperated on; recurrence after 3 y: proton radiotherapy
Dural	Persistent III dysfunction L
	1 y After operation proton radiotherapy; no recurrence 3 y after operation
Dural	Dysarthria, L hemiparesis and abscess cerebral, epilepsy; 4 months later recurrence
	Recurrence after 8 y
	Recurrence after 2 y; death 19 y after diagnosis
	Three times reoperated on; postoperative V, VII, IX, and XI dysfunction; epilepsy
	Increased paresis and dysphasia
Dural and cerebral	No surgical treatment
	Reoperation 1 y later, death 11 y after diagnosis
	Total hearing loss AD and VII dysfunction R; later stereotactical radiotherapy
Dural	Decreased visual acuity OD and hearing AD; hypaesthesia R face; no recurrence 3 y after operation

the preferable location of chondrosarcoma in the petrosal part of the skull base. A more lateral localisation explains initial VIIIth nerve dysfunction. Cerebral lesions caused by intradural and intracerebral expansion were reported in 30 cases. Most cases were described as orginating from the skull base (table 2), possibly from remnants of embryonal cartilage. However, a few were reported to originate from dural tissue, suggestive of metaplasia of meningeal fibroblasts.[2]



Age distribution for the different pathological subtypes of skull base chondrosarcomas.

On radiological examination, plain skull radiography showed only bone destruction and calcifications. Before 1980, angiography was used to evaluate the intracranial extension. Skull CT with intravenous contrast also disclosed bone destruction and calcification with more detailed demarcation of the tumour extension.

Skull MRI with administration of gadolinium DTPA resulted in even better tumour demarcation and visualisation of dural extension. The anatomical relations of the tumour with main vessels such as the carotid arteries and optic nerves are important guides for the extension of neurosurgical extirpation.[39]

Bone biopsy was the main diagnostic tool. The pathological classification of the subtypes grade I - III is based on differences in characteristics such as nuclear size, cellularity, mitotic rate, and frequency of lacunae with multiple nuclei.[43] Our study of 177 patients in the literature and 15 Dutch patients disclosed no grade III chondrosarcoma. In the mesenchymal subtype, primitive spindle cells are present.[44] The myxoid type is composed of strings of rounded cells in a more or less myxoid matrix.[45]

With the help of tumour markers such as vimentin, cytokeratin, and S100, the chondrosarcoma can be differentiated from chordoma. Chordomas lack vimentin immunoreactivity and chondrosarcomas fail to express cytokeratin. S-100 protein expression is present in both.[45]

In the literature, mesenchymal and myxoid subtypes are classified separately from the conventional type I - III gradation. Lichtenstein and Bernstein considered the mesenchymal chondrosarcoma as a seperate subtype.[44] Evans *et al* described a subgroup of grade III chondrosarcoma containing large areas exhibiting a spindle cell pattern, but with a mitotic rate well in excess of minimum criteria for grade III.[43] Although not explicitly mentioned, their description fits the definition of mesenchymal chondrosarcoma. It is our opinion that on the basis of this finding, at least the mesenchymal chondrosarcoma should be considered as a separate subtype.

Mesenchymal chondrosarcomas mainly occurred in the younger age group (10–30 years). The grade I chondrosarcoma had no clear age preference.

Very little data were available on the presence of dural invasion in skull base chondrosarcoma. The more malignant mesenchymal chondrosarcoma had a tendency towards a malign growth pattern which is illustrated by the relatively high frequency of extension into dural and cerebral tissue. In our own series (15 patients), dural invasion was present in five cases: three of these were grade I and two grade II chondrosarcoma.

Metastases of chondrosarcoma with a primary localisation in other parts of the body were found in 10% of grade II and 71% of grade III tumours.[43] Metastases from the skull base were mentioned by Hassounah et al in five

Table 3 Results of radiotherapy in 108 patients with low grade chondrosarcoma of the cranial base, treated with charged particles

Reference	*Patients*	*Follow up (months)*	*Particles*	*Dose (GyE)*	*LC-5 (%)*	*SV-5 (%)*	*Complication rate (%)*
Castro *et al*[38]	27	4–191 (median 51)	Helium, neon	60–80 (median 66)	78	83	41 (77–86) 20 (87–92)
Munzenrider *et al*[46]	81	2–187 (median 37)	Proton	62.8–77.4 (median 68.5)	91	94	13 (auditory) 12 (endocrine) 10 (brain) 6 (visual)

LC-5 = local control rate at 5 y; SV-5 = survival rate at 5 y; GyE = Gray equivalent.

of 50 patients.[4] We were not able to find other cases with metastases.

Neurosurgery is one of the treatment options. In 53% of neurosurgically treated patients recurrence of the tumour was found (mean interval 32 months). The high recurrence rate is caused by partial resection due to the proximity of critical neuronal and vascular structures.

Several studies describe neurosurgical procedures and their results in treatment of intracranial chondrosarcoma.[18 34 41] Up to nine different surgical approaches are possible, often combined or in stages. Macroscopical total resection was accomplished in 56%-67% of cases. Postoperative radiotherapy was given in 20%-44% of the patients.

Gay and Sekhar reported on 60 patients with low grade cranial base chondrosarcoma[14] and chordoma.[41 46] Fifty percent of these patients were treated previously elsewhere. All were operated on and total or near total resection was achieved in 67% of cases. Twenty per cent of the patients received radiotherpy postoperatively. They found a recurrence free survival rate at five years of 65%. The most frequent complication of the operation was leakage of CSF (30%). During follow up two patients (3%) died because of complications of radiotherapy and three (5%) because of systemic complications of surgery.

Risk of recurrence of tumour growth was found to be greater in patients who were already operated on elsewhere and in the case of only partial resection.

In general, an optimal tumour removal in one operation was advocated, because repeated surgical intervention has risks of tumour progression, development of scar tissue, and secondary spread of tumour cells.[18 34 41]

Radiotherapy is another treatment for these tumours in the direct vicinity of essential structures. The anatomical close relation between the tumour and these critical normal structures limits the dose that can be delivered with conventional radiation treatment. Charged particle radiotherapy combined with three dimensional treatment planning results in superior dose distribution that allows delivery of high tumour dose with acceptable dose to the normal tissues.

Table 3 shows the results of the treatment of low grade chondrosarcoma of the skull base with combined proton and photon radiotherapy and with helium or neon radiotherapy.[38 46] Local control rates of 78%–91% and survival rates of 83%-94%, both at five years, were achieved.

The treatment related morbidity ranged from 6% (visual complications) to 13% (auditory complications) in series of chondrosarcomas (81cases) and chordomas (113 cases) of both the skull base and cervical spine.[46] Castro et al reported a decline in occurrence of all radiotherapy complications from 41% in the period before 1986 to 20% after 1986, demonstrating the impact of improved imaging and treatment planning techniques.[38] However, in the period 1977–92, five of 85 disease free patients (5%) died due to complications of therapy.

Despite the high rates of local success of charged particle radiotherapy and the fact that local recurrence always led to deterioration of the neurological condition, morbidity and mortality are considerable and should be taken into account when offering this treatment to patients.

Up to now, charged particle radiotherapy can only be carried out in highly specialised centres. It is our opinion however, that the role of radiotherapy in the treatment of skull base chondrosarcoma, possibly in combination with surgery, in the years to come will grow.

Skull base chondrosarcomas are tumours that should be considered in cases of unexplainable cranial nerve dysfunction and other associated symptoms. The reported interval between the first symptoms and moment of diagnosis was often long. In most reports important data in defining the natural history of a chondrosarcoma were missing. Also, pathological classification should be given in more detail. In comparison with neurosurgical, mostly partial, tumour resection, charged particle radiotherapy seems to give better follow up results in terms of five year survival. Both neurosurgery and radiotherapy can cause treatment related side effects that should influence therapy choice in the individual patient.

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